REMARKS

I. Prosecution History and Explanation of Amendments.

The application as filed contained 37 claims. On May 4, 2001 the Applicants filed a preliminary amendment canceling claims 1-37 and adding claims 38-96. In an official communication (Paper No. 11) date October 2, 2002, claims 38-96 were subjected to a restriction requirement. In a responsive Response to Restriction Requirement (Paper No. 12) filed on November 4, 2002, the Applicants elected with traverse to prosecute the invention of Group I, claims 38-52 and 71-80, directed to an isolated polynucleotide as set forth in SEQ ID NO: 1. At the time of issuance of the outstanding Office Action, claims 38-96 were pending in the application. In an Office Action dated April 29, 2003, the restriction requirement of January 29, 2003 was made final; claims 82-92 and 95-96 were withdrawn from consideration; and claims 38-81 and 93-94 were rejected variously under 35 U.S.C. §§101, 102 and 112, first paragraph.

In this response claims 38-96 have been canceled in favor of new claims 97-155. No new matter is introduced thereby. A claim correlation chart is attached as Appendix 1. The application now presents 32 independent claims (97, 98, 100-103, 105-108, 110-113, 115-118, 120-123, 125-128, 130-133, 135-136) from which all the remaining claims depend. Each of independent claims 97, 98, 100-103, 105-108, 110-113, 115-118, 120-123, 125-128, 130-133, 135-136 present different aspects of the invention. Specifically, claims 97, 98, 102, 103, 107, 108, 112, 113, 117, 118, 122, 123, 127, 128, 132, and 133 correspond to original claims 61-65 and recite an isolated human collectin polypeptide consisting of a region of the amino acid sequence of SEQ ID NO:2 wherein one or more amino acid(s) in the amino acid sequence may be deleted, substituted and/or added as long as the protein is still encoded by a polynucleotide that hybridizes under particular conditions. Support for these hybridization conditions as recited in the claim can be found on page 5, lines 1-9 and in Example 3. New independent claims 100, 101, 105, 106, 110, 111, 115, 116, 120, 121, 125, 126, 130, 131, 135, and 136 corresponds to original claim 39, 42, 45, 48, and 51 and recite an isolated polynucleotide consisting of a region in the nucleotide sequence of SEQ ID NO:1.

In paragraph 2 of the Office Action, the Patent Office objected that the title of the invention was not descriptive. In response, Applicants have amended the title to remove the word "novel" and elaborate on the term "collectin" as suggested by the Patent Office.

Applicants do not intend by these or any amendments to abandon subject matter of the claims as originally filed or later presented, and reserve the right to pursue such subject matter in continuing applications.

THE CLAIM REJECTIONS UNDER 35 U.S.C.§101 SHOULD BE WITHDRAWN

On page 5 of the Office Action, the Patent Office rejected claims 38-81 and 93 and 94 under 35 U.S.C. § 101 for allegedly lacking a specific, substantial, and credible, or a well established utility. The Patent Office acknowledged that the claimed nucleic acid molecules of the instant application encode scavenger receptor-like polypeptides (*see* Ohtani *et al., J. Biol. Chem.* 276, pp.44222-44228 (2001) and Nakamura *et al., Biochem. Biophys. Res. Commun.* 280, pp.1028-1035 (2001)), but asserted that the specification does not teach any functional characteristics of the human nucleotide sequence of SEQ ID NO: 1 or amino acid sequence of SEQ ID NO: 2. The Applicants respectfully traverse.

The premise of the rejection in this case is unsound because one of skill in the art is aware that substantial differences in primary structure exist between members of the collectin family of proteins, and yet the family members share a common function of increasing immunity against various microorganisms, including bacteria and viruses. The Patent Office acknowledged that of the known collectins, the polypeptide comprising SEQ ID NO:2 is most homologous (35 % identity) to SP-D, a collectin found in pulmonary surfactant capable of binding microorganisms and stimulating chemotaxis of phagocytes and production of oxygen radicals. The 35% identity between the polypeptide comprising SEQ ID NO:2 and SP-D is comparable to that observed for other family members. The % identity between SP-D and SP-A, two well-known members of the collectin family, is only 28% identity. This alignment is indicated in Figure 5 and page 29, line 29 through page 30, lines 1-4 of the specification.

Those skilled in the art are aware of structural signature sequences that identify a sequence as an collectin family member, notwithstanding the sequence divergence that is characteristic of the family. For example, the collectin family of proteins are characterized by the combination of a Ca^{2+}-dependent carbohydrate recognition domain (CRD) with a collagen-like region. Importantly, the CRDs have 4-6 cysteine residues which form disulfide linkages, while the collagen-like regions consist of the amino acid units of $(Gly\text{-}X\text{-}Y)_n$ which form triple-helix-based subunits. This triple helix-based subunit then becomes the basis for forming oligomers, such as trimers, tetramers, and hexamers of the protcin.

Collectins do not have higher ordered structural features, sueh as the trans-membrane region, leucine-zipper region region b, and α-coiled region which differentiate them structurally and functionally from the scavenger receptor proteins cited by the Patent Office. In addition, scavenger receptor proteins cannot take on an oligomeric form characteristic of collectins.

Referring to the claimed invention, the polypeptide of SEQ ID NO: 2 (encoded by the claimed polynucleotide of SEQ ID NO: 1 contains a CRD that contains six cysteines like those known to be presenl in the collectin family proteins and identify a protein as a family member as well as the amino acid sequence of Gly-Pro-Asp which is a carbohydrate specific motif. Likewise the polypeptide of SEQ ID NO: 2 (encoded by the claimed polynucleotide of SEQ ID NO: 1 contains a collagen-like region consisting of the amino acid sequence of $(Gly\text{-}X\text{-}Y)_n$ characteristic of collectins.

Furthermore, the specification notes that collectins may be used as medicines because of their known anti-viral activity. (*See* page 2, lines 13-16). Collectins, such as conglutinin and mannan-binding protein, inhibit infection and hemagluination activity of H1 and H3 Type Influenza A viruses (*See* page 2, lines 1-2). Because collectins are useful anti-viral agents, they could be useful for preventing or treating infectious diseases. Thus, the claimed collectin polynucleotide and polypeptide in the instant application have demonstrated credible, specific, and substantial utility because the collectins can be used in a variety of real world contexts to combat a number of infectious diseases. Accordingly, Applicants respectfully request that the rejection of claims 38-81 and 93-94 under 35 U.S.C. § 101 for

lack of utility has been overcome and should be withdrawn and a rejection of new claims 97-155 on the same grounds would be improper

THE CLAIM REJECTIONS UNDER 35 U.S.C.§112, FIRST PARAGRAPH (LACK OF ENABLEMENT) SHOULD BE WITHDRAWN

On page 8 of the Office Action, the Patent Office rejected claims 38-81 and 93 and 94 under 35 U.S.C. § 112, first paragraph, alleging the claimed invention is not supported by either a specific and substantial or a well established utility, the specification allegedly did not enable one skilled in the art to use the claimed invention without undue experimentation. As explained in detail in the preceding section, the application teaches specific, substantial, and credible utilities related to enhancing immunity against various microorganisms including bacteria and viruses, specifically how to use polynucleotides (or encoded polypeptides) of the invention as possible anti-bacterial or anti-viral agents. Thus, this rejection should be withdrawn, for reasons outlined in the preceding section.

On page 8 of the Office Action, the Patent Office also rejected claim 94 under 35 U.S.C. § 112, first paragraph, alleging the specification does not reasonably enable one skilled in the art how to use the transgenic non-human animal of claim 94 because one skilled cannot predict the phenotype arising from insertion or deletion of even a well-characterized gene for each and every transgenic animal. Applicants believe that this rejection of claim 94 is based on the premise that claim 94 encompasses the use of transgenic animals other than transgenic mice. Applicants believe that in view of the teachings of the specification those of skill in the art would be able to produce any transgenic non-human animal as a disease model for the function and regulation of collectins and collectin derivatives. However, in order to expedite prosecution of the instant application, claim 94 has been replaced with claim 156 which claims transgenic mice subject matter.

Given the detailed teachings of the specification and the level of skill in the art, it is well within the skill of artisans practiced in this field to prepare the transgenic mice of the present invention as a matter of routine practice and to use such mice in screening assays of the claimed invention. (*See* Example 14). Applicants believe that the amendment

to the claims to recite transgenic mice is consistent with the guidance from the Patent Office in the Office Action as to the subject matter enabled by the specification. In view of the foregoing, Applicants respectfully submit that the specification and claims are in full compliance with enablement requirement of 35 U.S.C. §112, first paragraph. Therefore, Applicants request that the rejections be withdrawn and the claims be reconsidered for allowance.

THE CLAIM REJECTIONS UNDER 35 U.S.C.§112, FIRST PARAGRAPH (LACK OF WRITTEN DESCRIPTION) SHOULD BE WITHDRAWN

On page 10 of the Office Action, the Patent Office rejected claims 38-81 and 93-94 under 35 U.S.C. § 112, first paragraph, alleging the specification does not reasonably convey to one skilled in the art that the inventors had possession of the genus of "any and all nucleic acids and polypeptides, as well as products comprising said nucleic acids and polypeptides and methods of using said nucleic acids and polypeptides." The Patent Office concludes that the specification does not teach functional or structural characteristics of the nucleic acid molecules in the context of a cell or organism. The Patent Office seems to acknowledge that the specification provides written descriptive support with respect to SEQ ID NO: 1 and the encoded polypeptide of SEQ ID NO: 2, but only does not provide support for an genus that encompasses species that were not in Applicant's possession at the time of filing (i.e. Ohtani et al.; Nakamura et al., *Biochem. Biophys. Acta*; and Nakamura et al. *Biochem. Biophys. Res. Commun.*).

In addition on page 12 of the Office Action, the Patent Office rejected claims 53-56, 58-60, 66-68, 73-75, 78-79, and 81 under 35 U.S.C. § 112, first paragraph, alleging the specification does not reasonably convey to one skilled in the art that the inventors had possession of the "broad class of nucleic acids and polypeptides" because the specification does not teach sufficient stringency of the hybridization conditions to have sufficient homology with the disclosed nucleic acids and polypeptides.

The Applicant's believe that these rejections have been obviated by the amendments. The amended claims are directed to sequences that are supported in the

specification and to specific hybridization conditions. Therefore, the basis for these rejections does not apply to new independent claims 97, 98, 100-103, 105-108, 110-113, 115-118, 120-123, 125-128, 130-133, and 135-136, which are directed to an "isolated human collectin polypeptide consisting of particular regions in the amino acid sequence of SEQ ID NO:2; which may include one or more amino acid(s) deletions, substitutions and/or additions as long as it is encoded by a polynucleotide which hybridizes under particular hybridization conditions.

As the Patent Office recognizes, the issue of written description involves the question of whether the specification shows that the Applicants had possession of the claimed invention. There is clearly written descriptive support in the specification for sequences that consist of particular regions of the nucleotide sequence SEQ ID NO: 1 and amino acid sequence SEQ ID NO: 2 (see specification at page 4, lines 11-34). Moreover, the specification teaches isolated human collectin polypeptide consisting of regions of SEQ ID NO: 2 that is encoded by a polynucleotide which hybridizes under the following hybridization conditions: hybridization at 55°C in a hybridization solution comprising 5 X SSC, 1% blocking agent, 0.1% N-lauroyl sarcosine and 0.02% SDS; and washing at 55°C in a wash solution comprising SSC/0.1% SDS, wherein the polypeptide comprises a Ca^{2+}-dependent carbohydrate recognition domain (CRD) and a collagen-like region. (*See* page 5, lines 1-11, Example 3).

Hybridization conditions are a common and accepted way to define a genus of polynucleotides. The claimed invention meets the requirements the USPTO's Training Materials for the Interim Written Description and Utility Guidelines as set forth in Example 9. Examples 1-4 of the specification indicate that the claimed polynucleotide can be obtained by the steps comprising: 1) identifying molecules with highly conserved regions with the collectin set out in SEQ ID NO:3 (see Example 1), preparing probes from the clones so obtained for screening (see Example 2), screening by hybridization of a cDNA library from human placenta for complementary polynucleotides (see Example 3), and determining the base sequences of the cDNA (see Example 4). Hybridization takes place under the following conditions: hybridization at 55°C in a hybridization solution comprising 5 X SSC, 1% blocking agent, 0.1% N-lauroyl sarcosine and 0.02% SDS; and washing at 55°C in a wash

solution comprising 2 X SSC/0.1% SDS. It should be noted that the Applicant succeeded in Example 3 through screening-by-hybridization to isolate polynucleotides which hybridize with the probes prepared in Example 2. From this process, the specification teaches one of ordinary skill in the art how to isolate the polynucleotides of the claims. Protein encoded by the polynucleotides of the claims have been show to have the same activities (e.g. anti-viral activity, immuno-enhancing activity) as known collectins. The claims are directed to polynucleotides that have the definite sequence properties to hybridize under the specified conditions and therefore the rejection should be withdrawn

Further and as noted above, claims 100, 101, 105, 106, 110, 111, 115, 116, 120, 121, 125, 126, 130, 131, 135, and 136 recite an isolated polynucleotide consisting of a region in SEQ ID NO:1. Support in the specification for polynucleotides consisting of SEQ ID NO:1 can be found at page 4, lines 11-34. Thus, the specification provides ample written descriptive support for the invention of new claims 97-155.

In light of the foregoing amendments, the rejection of claims 38-81, 93 and 94, under 35 U.S.C. § 112, first paragraph, for lack of enablement and written description, has been overcome and should be withdrawn, and a rejection of new claims 97-155 on the same grounds would be improper.

THE CLAIM REJECTIONS UNDER 35 U.S.C. §102 SHOULD BE CLARIFIED OR WITHDRAWN

On page 14 of the Office Action, the Patent Office rejected claims 38-57, 71-81 and 93 under 35 U.S.C. § 102, first paragraph, as being anticipated by "SEQ ID NO: 11" in WO/98/55617 published December 10, 1998. Applicants respectfully traverse.

WO/98/55617 only discloses four sequences, SEQ IDS NO: 1-4. WO/98/55617 make no reference to a SEQ ID NO: 11. Because it is not clear what sequence the Patent Office is referring to in the rejection, the Applicant's respectfully request clarification or withdrawal of the rejection.

CONCLUSION

For all of the foregoing reasons, the applicant's respectfully request that the rejections should now be withdrawn and an early notice of all pending claims is respectfully solicited. Should the Patent Office wish to discuss any issues of form or substance in order to expedite allowance of the pending application, he is invited to contact the undersigned attorney at the number indicated below. If there are any additional fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 50-0310.

Dated: October 29, 2003

Respectfully submitted,

By _____

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